REMARKS

Status of the Claims

Claims 273 to 300 were pending. Claims 287-292, 299 and 300 have been withdrawn from consideration pursuant to Restriction and Election of Species Requirements that have been made FINAL. Claim 273 has been amended to specify that the DNA-binding domain is a zinc finger DNA-binding domain, as described throughout the specification as-filed. Accordingly, claims 295 and 298 have been canceled, without prejudice or disclaimed. Claims 273, 275, 279, 293 and 294 have been amended to remove the terms "DBD" and "DBD recognition element." Thus, claims 273 to 295, 296, 297, 299 and 300 are pending as shown above.

Restriction/Election

Restriction as between Group I (claims 273 to 298) and Group II (claims 299 and 300) has been made FINAL on the grounds that "a population of host cells of the claims of Group I could produce a fusion protein containing an activation tag, wherein the fusion proteins could be used to produce antibody against the said activation tag." (Office Action, paragraph 2). Applicants again submit that a Restriction Requirement cannot be maintained on the grounds that a skilled artisan would go the trouble of making a population of host cells as claimed containing multiple components in order to make an antibody to one of these many components, namely an activation tag. In any event, even if this assertion was credible, Applicants reiterate that the methods of Group II depend from claim 273 of Group I and, as such, include all the limitations of the cells of Group I. Thus, rejoinder is in order.

Similarly, the election of species requirement has also been made FINAL on the grounds that Dove et al. "teach that interaction trap systems, were well-known in the art, and that they differ in the specifics, including DNA binding domains, reporter genes, activation domains." (Office Action, page 3). For the reasons detailed below, Dove et al. does not teach cell populations as claimed, in which at least 10^7 unique pairs of a binding site and a fusion protein are represented in the population of host cells. Thus, because the claims require at least 10^7 unique pairs of binding site-fusion proteins, a search for any host cell (prokaryotic or eukaryotic) comprising a fusion protein including any activation tag and any reporter gene would necessarily and inevitably reveal art relevant to all allegedly distinct species.

Based on the foregoing, Applicants request reconsideration of the Restriction and Election of Species requirements and submit that all claims should be examined together.

Applicants expressly reserve their right under 35 USC § 121 to file one or more divisional applications directed to the nonelected subject matter during the pendency of this application. Applicants also reserve their right, pursuant to 37 C.F.R. §§ 1.144 and 1.181, to petition this requirement at any time during the pendency of this application, prior to appeal.

Information Disclosure Statement

The Office Action indicated that the IDS filed with the application did not comply with 37 C.F.R. § 1.98(a)(2) in regards to citations B4-B8 on the grounds that these references could not be found in prior Application Serial No. 09/990,762. (Office Action, paragraph 6).

Applicants note that the instant application is a continuation of application 09/858,852 (now abandoned) rather than 09/990,762, as set forth in the Office Action. Copies of references B4-B8 were received by the Office in the parent case (copies of the stamped postcard and IDS in parent application no. 09/858,852 are attached hereto).

Accordingly, Applicants request that these references be considered by the Office and that the PTO/SB/08A form be initialed and signed indicating consideration of these references.

Specification

The specification was objected to for failing to identify sequences in the drawings or Brief Description of the Drawings. (Office Action, paragraph 7). In addition, an update to the priority information was requested. (Office Action, paragraph 8).

As shown above, the specification has been amended to include sequence identifiers at the appropriate location and to include the patent number of the parent application. Accordingly, the objections have been obviated.

Claim Objections

Claim 279 was objected to under 37 C.F.R. § 1.75(c) as allegedly being of improper dependent form. (Office Action, paragraph 9).

In response, Applicants have amended claim 279 to depend from claim 273. Thus, the objection has been obviated.

35 U.S.C. § 112, 2nd Paragraph

Claims 273-286 and 293-298 were rejected under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite. (Office Action, paragraph 11). In particular, claim 273 was alleged to be incomplete for omitting essential structural cooperative relationships as follows: the polynucleotide encoding a fusion protein; the transcriptional regulatory sequence, and the reporter gene operably linked to the transcriptional regulatory sequence. *Id.* Claim 273 was also alleged to be indefinite for reciting "DBD" and "DBD recognition element as well as for reciting "a DNA binding domain" in lines 7 and 10. *Id.* Claim 275 was rejected for reciting "the desired level of expression" and claim 279 was rejected for insufficient antecedent basis for the term "intermediary peptide." *Id.*

Applicants submit that the metes and bounds of claim 273, as amended above, are entirely clear to the skilled artisan. With regard to the alleged omissions of "structural cooperation," claim 273 plainly sets forth all the structural relationships necessary to particularly point out the claimed population of cells, including that the reporter gene is operably linked to the transcriptional regulatory sequence (part (c) of claim 273); the components of the fusion protein (part (a) of claim 273); and the relationship between the fusion protein and the transcriptional regulatory sequence-reporter gene construct (part (c) of claim 273). The claim is drawn to a population of host cells comprising the various recited components, and the relationships between the various components of the host cell are clearly set forth.

In addition, the abbreviation "DBD" and the recitation "DBD recognition element" have been removed from claim 273. Finally, Applicants note that the term "DNA binding domain occurs only once on line 7. Thus, claim 273 and claims dependent therefrom are clear and definite.

Claims 274 and 279 have been amended to provide sufficient antecedent basis and to obviate the rejections as set forth. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, 2nd paragraph is in order.

35 U.S.C. § 103(a)

Claims 273-285 and 293-298 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over U.S. Patent No. 5,925,523 (hereinafter "Dove") in view of Jappelli et al. (1999) *Biochem. Biophys. Res. Commun.* 266:243-247 (hereinafter "Jappelli"). (Office Action, paragraph 13). Dove was cited as allegedly teaching a population of host cells including all the elements of the claims except for "at least 10^7 unique pairs" as recited in claim 273. Jappelli was cited for allegedly teaching methods of identifying dimerizing polypeptides in *E. coli* using a library comprising 10^{10} members. *Id.* It was alleged that it would have been obvious to combine Dove and Jappelli because Jappelli states that identification of novel sequences may be interesting for protein engineering and because Dove teach using transfected host cells to screen polypeptide libraries as part of an interaction trap system. *Id.*

Claim 286 was also rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Dove in view of Jappelli and further in view of U.S. Patent No. 5,885,779 (hereinafter "Sadowski"). (Office Action, paragraph 14). Dove and Jappelli are cited as above and Sadowski was cited for disclosing varying concentrations of 3-aminotriazole to control growth in host cells. *Id.*

Applicants submit that a *prima facie* case of obviousness has not been set forth. The assertion that making a population of host cells as claimed, comprising a library of at least 10^7 members, is somehow trivial and/or obvious over the references is completely unsupported and, in fact, contradicted, by the evidence of record. Dove does not teach or suggest host cells comprising libraries of at least 10^7 members, as claimed. Indeed, the as-filed specification clearly details that Dove's teachings do not extend to large libraries as claimed (see, page 3, line 34 to page 4, line 6, emphasis added; page 5, line 25 to page 6, line 2, emphasis added):

> More recently, a prokaryote-based interaction trap assay has been developed. See, for example, U.S. Pat. No. 5,925,523 [Dove]. ... Because bacteria (*E. coli* in particular) have a much higher relative transformation efficiency (typically 10^9 or greater) than yeast, the description of prokaryotic-based one- and two-hybrid systems would appear to address the library size restrictions of the yeast systems. However, although higher transformation efficiencies are possible in *E. coli*, a significant deficiency of the prior art is that it does not make clear which, if any, reporter gene(s) have the characteristics required for use in the analysis of libraries larger than 10^7 in size. ...

> ...Even in bacteria where very high transformation efficiencies are possible, examination of 10^9combinations would only allow one to examine two libraries each comprised of only 33,000 candidates. In addition, since transformation requires pre-treatment of cells (e.g.--washing and resuspension in divalent cation solutions) and multiple protocol steps (e.g.--heat shock, addition of medium, recovery), it is not easily adaptable for automation. ... In this way, a large number of combinations can be simply and rapidly tested, bypassing the need for labor-intensive transformation experiments when crossing the libraries. See Uetz et al. (2000) Nature 403:623 627 and Walhout et al. (2000) Science 287:116 122. Prokaryotes (and *E. coli* in particular) replicate asexually, and U.S. Pat. No. 5,925,523 [Dove] and the existing literature do not teach how to perform analogous library mating experiments in the prokaryotic ITS.

Thus, Dove teaches away from a population of host cells as claimed, comprising at least 10^7 library members. Without the benefit of Applicants' disclosure, the skilled artisan would have had no motivation to combine Dove and Jappelli or Dove, Jappelli and Sadowski, as set forth in the rejection. Thus, the rejection is based on improper hindsight reconstruction and should be withdrawn.

Double Patenting

A. Claims 273-275, 282, 293, 294, 296 and 297

Claims 273-275, 282, 293, 294, 296 and 297 were rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 35 and 36 of Dove in view of Jappelli et al. (Office Action, paragraph 16). The rejection is essentially as set forth for 103(a) above. *Id.*

However, for a proper obviousness-type double patenting rejection, the Office must show that the conflicting claims are not patentably distinct from the reference claim(s). See, M.P.E.P. § 804(B), citing *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); and *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

In the instant case, the Office has not established and cannot establish that composition claims 273-275, 282, 293, 294, 296 and 297 (which require a library of at least 10^7 members) are patentably **in**distinct from method claims 35 and 36 of Dove. Not only is the size of the claimed

library not suggested by Dove and/or Jappelli, Applicants note that, given that the Patent Office invariable restricts compositions and methods claims, patentable **in**distinctness has not been established. Thus, the obviousness-type double patenting rejection cannot be sustained.

B. Claims 273-275, 282, 293-298

Claims 273-275, 282, 293-298 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-5 of copending Application No. 10/915,233 in view of Jappelli. (Office Action, paragraph 17).

Claims 1-5 of copending Application No. 10/915,233 are method claims and, accordingly, the Office has not shown that these claims are patentably **in**distinct from the composition claims as pending. Therefore, the obviousness-type double patenting rejection should be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance and request early notification to that effect. If the Examiner has any further issues or wishes to discuss any of the foregoing, he is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

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